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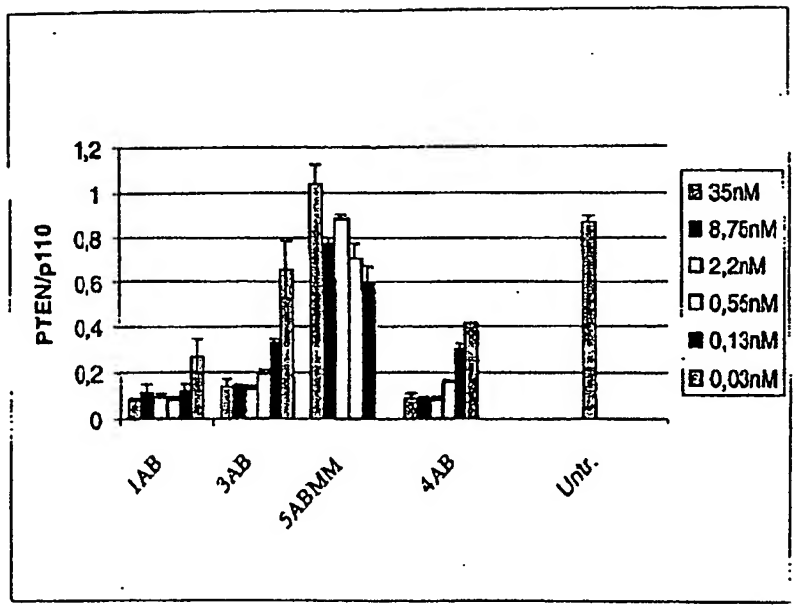
Atty. Dkt. No. 39078-0005
Title: INTERFERING RNA MOLECULES
Inventor: Klaus GIESE
Filed: August 5, 2003

Fig.3



3A

ONLY RNA WITH 2 DEOXY AT EACH END
1A 5'- cuccuuuuguuucugcuaacg-TT (1)
1B 3'-TT-gaggaaaacaaagacgauugc (2)

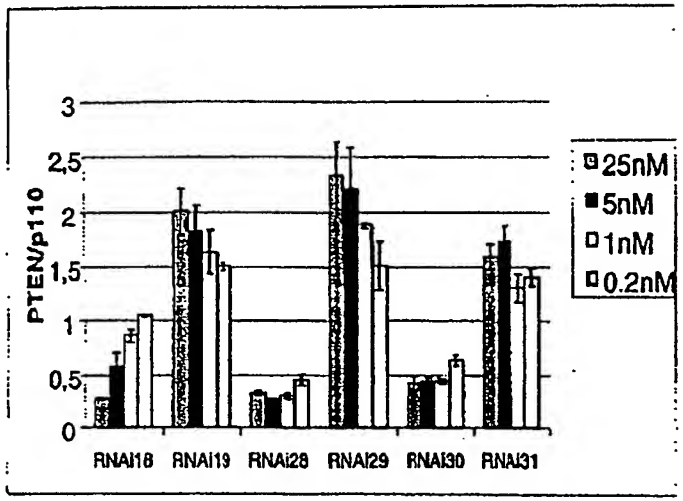
ONLY RNA WITH NH2 GROUPS AT EACH 3' END AND 2 DEOXY
3A 5'- cuccuuuuguuucugcuaacg-TT-NH2 (3)
3B 3'-NH2-TT-gaggaaaacaaagacgauugc (4)

ONLY RNA WITH INVERTED ABASIC AND 2 TT
4. 16153-iB (iB at the 3' ends)
4A 5'- cuccuuuuguuucugcuaacg-TT-iB (5)
4B 3'-iB-TT-gaggaaaacaaagacgauugc (6)

ONLY RNA WITH 2 DEOXY AT EACH END
5AMM 5'- cucauuuucuuugugcucacg-TT (7)
5BMM 3'-TT-gaguaaaagaaacacgagugc (8)

3B

4A



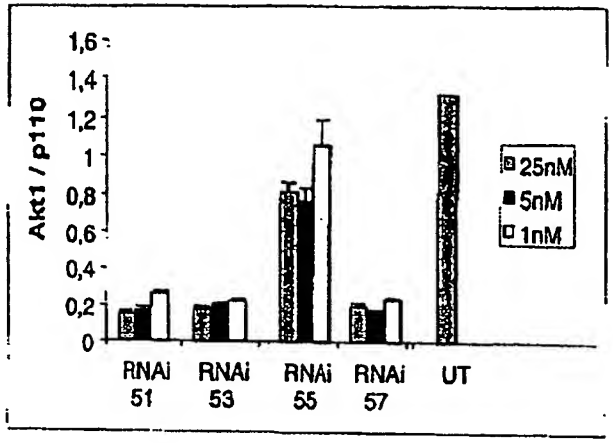
4B

18A	5'- cuccuuuuguuucugcuaacg-TT (9)
18B	3'-TT-gaggaaaacaaagacgauugc (10)
19A(MM)	5'- cucauuuucuuugugcucacg-TT (11)
19B(MM)	3'-TT-gaguaaaagaaacacgagugc (12)
28A	5'- cuccuuuuguuucugcuaacg- (13)
28B	3'- gaggaaaacaaagacgauugc- (14)
29A(MM)	5'- cucauuuucuuugugcucacg- (15)
29B(MM)	3'- gaguaaaagaaacacgagugc (16)
30A	5'-TT-cuccuuuuguuucugcuaacg- (17)
30B	3' -gaggaaaacaaagacgauugc-TT (18)
31A (MM)	5'-TT-cucauuuucuuugugcucacg- (19)
31B (MM)	3' -gaguaaaagaaacacgagugc-TT (20)

Fig. 4

Fig. 5

5A

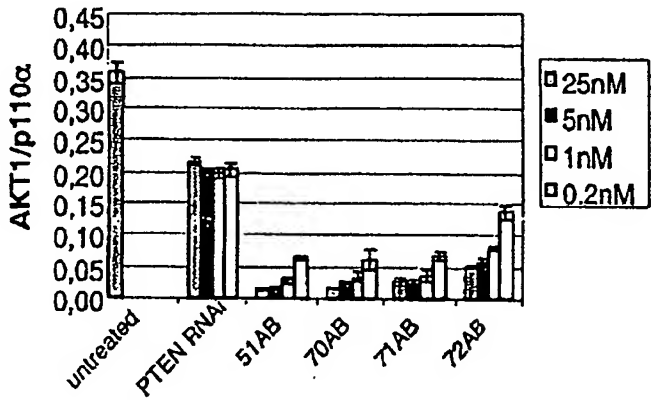


5B

51A	5'-	-ucuugauguacuccccucg-uu (21)	19nt 3'uu
51B	3'-	uu-agaacuacaugaggggagc- (22)	
53A	5'-	-ucuugauguacuccccucg-uu (23)	19nt 3'seq.specific RNA
53B	3'-	cc-agaacuacaugaggggagc- (24)	
55A	5'-	-cuugauguacuccccuc-gu (25)	17nt 3'seq.specific RNA
55B	3'-	ca-gaacuacaugaggggag- (26)	
57A	5'-	-ucuugauguacuccccucg-TT (27)	19nt 3'seq.specific DNA
57B	3'-	CC-agaacuacaugaggggagc- (28)	

Fig. 6

6A



6B

19nt(3'uu)

51A 5'- -ucuugauguacucccccucg-uu (29)
51B 3'- uu-agaacuacaugaggggagc- (30)

19nt (3'TT)

70A 5'- -ucuugauguacucccccucg-TT (31)
70B 3'- TT-agaacuacaugaggggagc- (32)

19nt with 1MM on both sites

71A 5'- -acuugauguacucccccucc-TT (33)
71B 3'- TT-ugaacuacaugaggggagg- (34)

19nt with 2MM on both sites

72A 5'- -aguugauguacucccccugc-TT (35)
72B 3'- TT-ucaacuacaugaggggacg- (36)

A

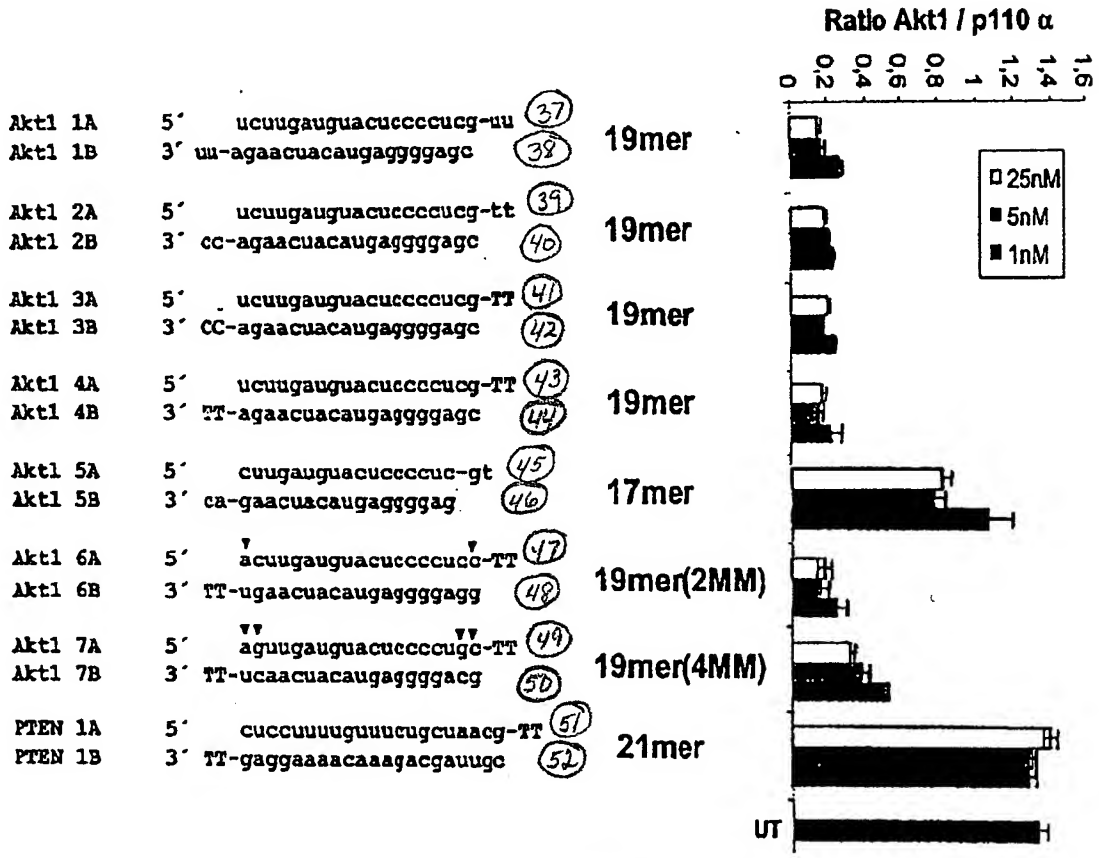

Ratio Akt1 / p110 α
0
0,2
0,4
0,6
0,8
1
1,2
1,4
1,6
25nM
5nM
1nM
Akt1 1A 5′ ucuugauguacucccccucg-uu (37)
Akt1 1B 3′ uu-agaacuacaugaggggagc (38)
19mer
Akt1 2A 5′ ucuugauguacucccccucg-tt (39)
Akt1 2B 3′ cc-agaacuacaugaggggagc (40)
19mer
Akt1 3A 5′ ucuugauguacucccccucg-TT (41)
Akt1 3B 3′ CC-agaacuacaugaggggagc (42)
19mer
Akt1 4A 5′ ucuugauguacucccccucg-TT (43)
Akt1 4B 3′ TT-agaacuacaugaggggagc (44)
19mer
Akt1 5A 5′ cuugauguacucccccuc-gt (45)
Akt1 5B 3′ ca-gaacuacaugaggggag (46)
17mer
Akt1 6A 5′ acuugauguacucccccucc-TT (47)
Akt1 6B 3′ TT-ugaacuacaugaggggagg (48)
19mer(2MM)
Akt1 7A 5′ aguugauguacucccccugc-TT (49)
Akt1 7B 3′ TT-ucaacuacaugaggggacg (50)
19mer(4MM)
PTEN 1A 5′ cuccuuuuguuucugcuaacg-TT (51)
PTEN 1B 3′ TT-gaggaaaacaaagacgauugc (52)
21mer
UT

Fig. 7

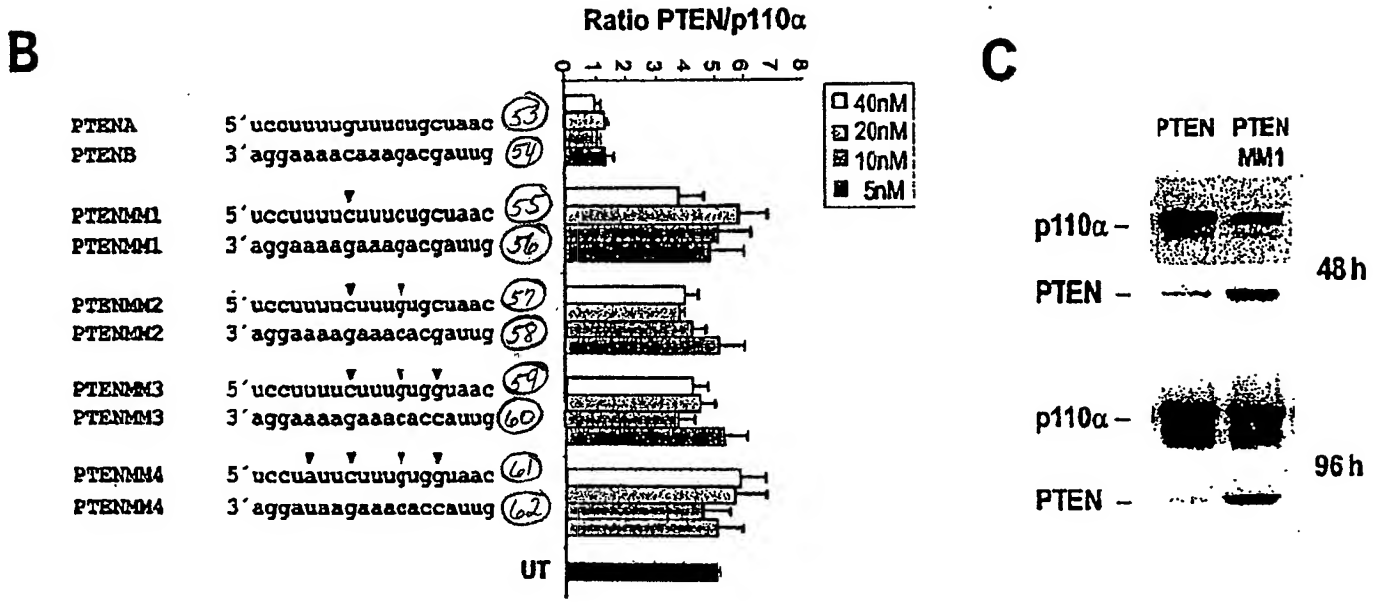

B
Ratio PTEN/p110α
0 1 2 3 4 5 6 7 8
40nM
20nM
10nM
5nM
PTENA 5´uccuuuuguuucugcuaac 53
PTENB 3´aggaaaacaaagacgauug 54
PTENMM1 5´uccuuuucuuucugcuaac 55
PTENMM1 3´aggaaaagaaagacgauug 56
PTENMM2 5´uccuuuucuuugugcuaac 57
PTENMM2 3´aggaaaagaaacacgauug 58
PTENMM3 5´uccuuuucuuugugguaac 59
PTENMM3 3´aggaaaagaaacaccauug 60
PTENMM4 5´uccuauucuuugugguaac 61
PTENMM4 3´aggauaagaaacaccauug 62
UT
C
PTEN
PTEN MM1
p110α –
PTEN –
48 h
p110α –
PTEN –
96 h

Fig. 7

Fig. 8'

8A

8B

Tuschl
18A 5'- cuccuuuguuucugcuaacg-TT (9)
18B 3'-TT-gaggaaaacaaagacgauugc (10)

inverted abasic on both ends and 2TT
24A 5'- iB-cuccuuuguuucugcuaacg-TT-iB (63)
24B 3'-iB-TT-gaggaaaacaaagacgauugc-iB (64)

NH2groups at both ends AND 2-deoxy
26A 5'- NH2-cuccuuuguuucugcuaacg-TT-NH2 (65)
26B 3'-NH2-TT-gaggaaaacaaagacgauugc-NH2 (66)

2'-O-Methyl modified with 2-deoxy at each end
79A 5'- cuccuuuguuucugcuaacg-TT (67)
79B 3'- TT-gaggaaaacaaagacgauugc (68)

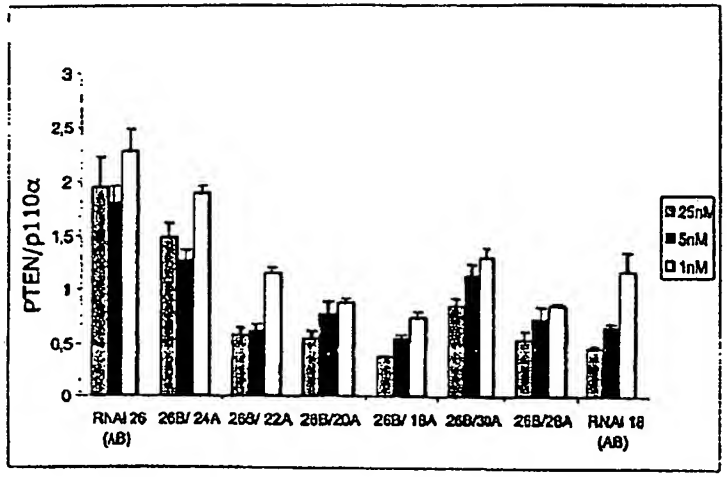
Only RNA
28A 5'- cuccuuuguuucugcuaacg- (13)
28B 3'- gaggaaaacaaagacgauugc- (14)

Only RNA with 2-deoxy at each 5' end
30A 5'-TT-cuccuuuguuucugcuaacg- (17)
30B 3'- gaggaaaacaaagacgauugc-TT (69)

NH2 groups at each 3'end and 2-deoxy
3A 5'- cuccuuuguuucugcuaacg-TT-NH2 (70)
3B 3'-NH2-TT-gaggaaaacaaagacgauugc- (71)

Fig. 9

9A



9B

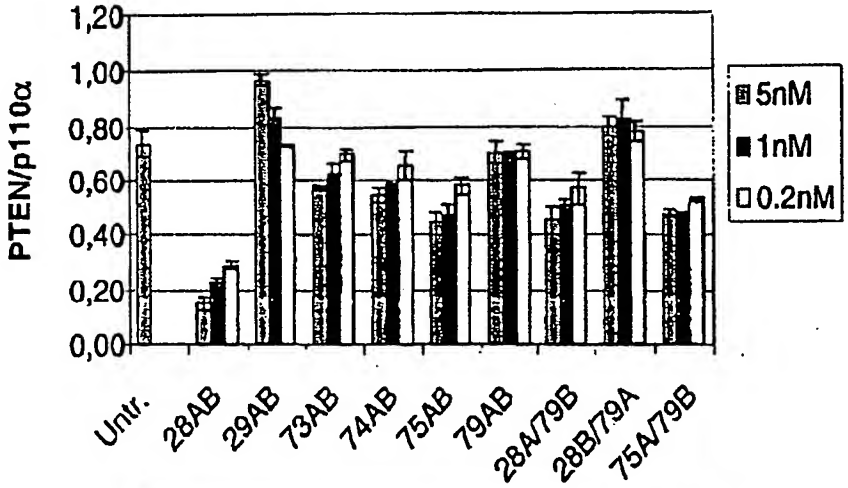
26A	5'- NH2-cuccuuuuguuucugcuaacg-TT-NH2 (72)
26B	3'-NH2-TT-gaggaaaacaaagacgauugc-NH2 (77)
24A	5'- iB-cuccuuuuguuucugcuaacg-TT-iB (73)
26B	3'-NH2-TT-gaggaaaacaaagacgauugc-NH2 (77)
22A	5'- cuccuuuuguuucugcuaacg-TT-iB (74)
26B	3'-NH2-TT-gaggaaaacaaagacgauugc-NH2 (77)
20A	5'- cuccuuuuguuucugcuaacg-TT-NH2 (75)
26B	3'-NH2-TT-gaggaaaacaaagacgauugc-NH2 (77)
18A	5'- cuccuuuuguuucugcuaacg-TT (78)
26B	3'-NH2-TT-gaggaaaacaaagacgauugc-NH2 (77)
30A	5'- TT-cuccuuuuguuucugcuaacg- (76)
26B	3'-NH2-TT-gaggaaaacaaagacgauugc-NH2 (77)
28A	5'- cuccuuuuguuucugcuaacg- (80)
26B	3'-NH2-TT-gaggaaaacaaagacgauugc-NH2 (77)
18A	5'- cuccuuuuguuucugcuaacg-TT (78)
18B	3'- TT-gaggaaaacaaagacgauugc (79)

9C

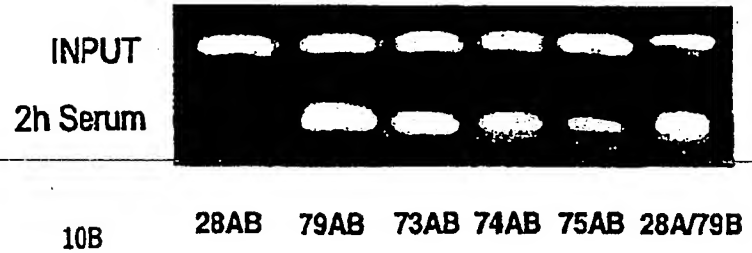
-nnnnnnnnnnnnnnn-tt NH2-nnnnnnnnnnnnnnn-NH2	functional
-nnnnnnnnnnnnnnn-tt-NH2 NH2-nnnnnnnnnnnnnnn-NH2	functional
NH2-nnnnnnnnnnnnnnn-tt-NH2 tt-nnnnnnnnnnnnnnn-tt	not functional

Fig. 10

10A



10B



10C

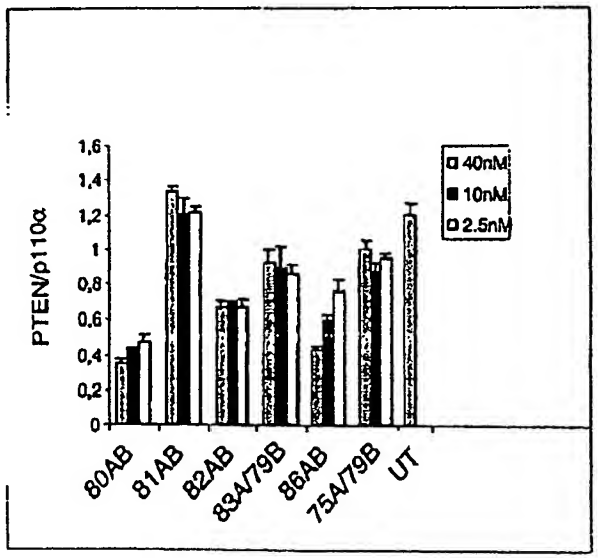
orig.

RNA Bold Italics represents 2'O-methyl

28A	5'-	cuccuuuuguuucugcuaacg-	13
28B	3'-	gaggaaaacaaagacgauugc	14
29A	5'-	cuccuuuucuuugugcuaacg	81
29B	3'-	gaggaaaacaaacacgauugc	82
73A	5'-	cuccuuuuguuucugcuaacg-	93
73B	3'-	-gaggaaaacaaagacgauugc-	94
74A	5'-	cuccuuuuguuucugcuaacg-	85
74B	3'-	-gaggaaaacaaagacgauugc-	86
75A	5'-	cuccuuuuguuucugcuaacg-	87
75B	3'-	-gaggaaaacaaagacgauugc-	88
79A	5'-	cuccuuuuguuucugcuaacg-	89
79B	3'-	-gaggaaaacaaagacgauugc-	90
28A	5'-	cuccuuuuguuucugcuaacg-	89
79B	3'-	-gaggaaaacaaagacgauugc-	90
79A	5'-	cuccuuuuguuucugcuaacg-	89
28B	3'-	gaggaaaacaaagacgauugc-	14
75A	5'-	cuccuuuuguuucugcuaacg-	87
79B	3'-	-gaggaaaacaaagacgauugc-	90

Fig. 11

11A



11C

RNA	Bold Italics represents 2'O-methyl		
80A	5'-	cuccuuuuguuucugcuaacg-	91
80B	3'-	-gaggaaaacaaagacgauugc-	92
81A	5'-	***cuccuuuug***uuucugcuaacg-	93
81B	3'-	-gaggaaaaca***aagacgauugc***-	94
82A	5'-	cuccuuuug***uuucugcuaacg***-	95
82B	3'-	***gaggaaaaca***aagacgauugc-	96
83A	5'-	cuccuuuu***guuucugcuaacg***	97
79B	3'-	-***gaggaaaacaaagacgauugc***-	90
86A	5'-	cuccuuuug***uuucugcuaacg***	98
86B	3'-	-***gaggaaaacaaagac***gauugc-	99
75A	5'-	cuccuuuug***uuucug***cuaacg-	100
79B	3'-	-***gaggaaaacaaagacgauugc***-	90

11B

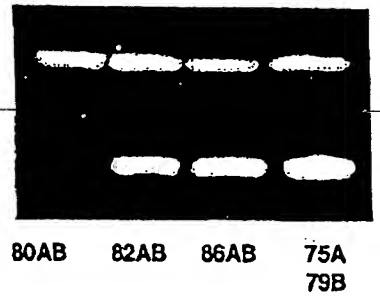
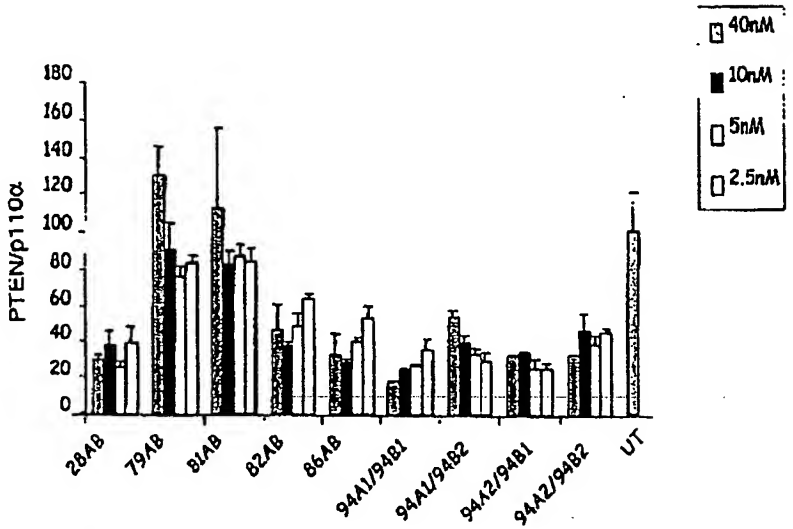


Fig. 12

12A



RNA Bold Italics represents 2' O-methyl

28A	5'-	cuccuuuuguuucugcuaacg- (101)	86A	5'-	cuccuuuuguuucugcuaacg- (109)
28B	3'-	gaggaaaacaaagacgauugc- (102)	86B	3'-	gaggaaaacaaagacgauugc- (110)
79A	5'-	cuccuuuuguuucugcuaacg- (103)	94A1	5'-	cuccuuuuguuucugcuaacg- (111)
79B	3'-	gaggaaaacaaagacgauugc- (104)	94B1	3'-	gaggaaaacaaagacgauugc- (112)
81A	5'-	cuccuuuuguuucugcuaacg- (105)	94A1	5'-	cuccuuuuguuucugcuaacg- (113)
81B	3'-	gaggaaaacaaagacgauugc- (106)	94B2	3'-	gaggaaaacaaagacgauugc- (114)
82A	5'-	cuccuuuuguuucugcuaacg- (107)	94A2	5'-	cuccuuuuguuucugcuaacg (115)
82B	3'-	gaggaaaacaaagacgauugc- (108)	94B1	3'-	gaggaaaacaaagacgauugc (116)
			94A2	5'-	cuccuuuuguuucugcuaacg (117)
			94B2	3'-	gaggaaaacaaagacgauugc (118)

12B

A

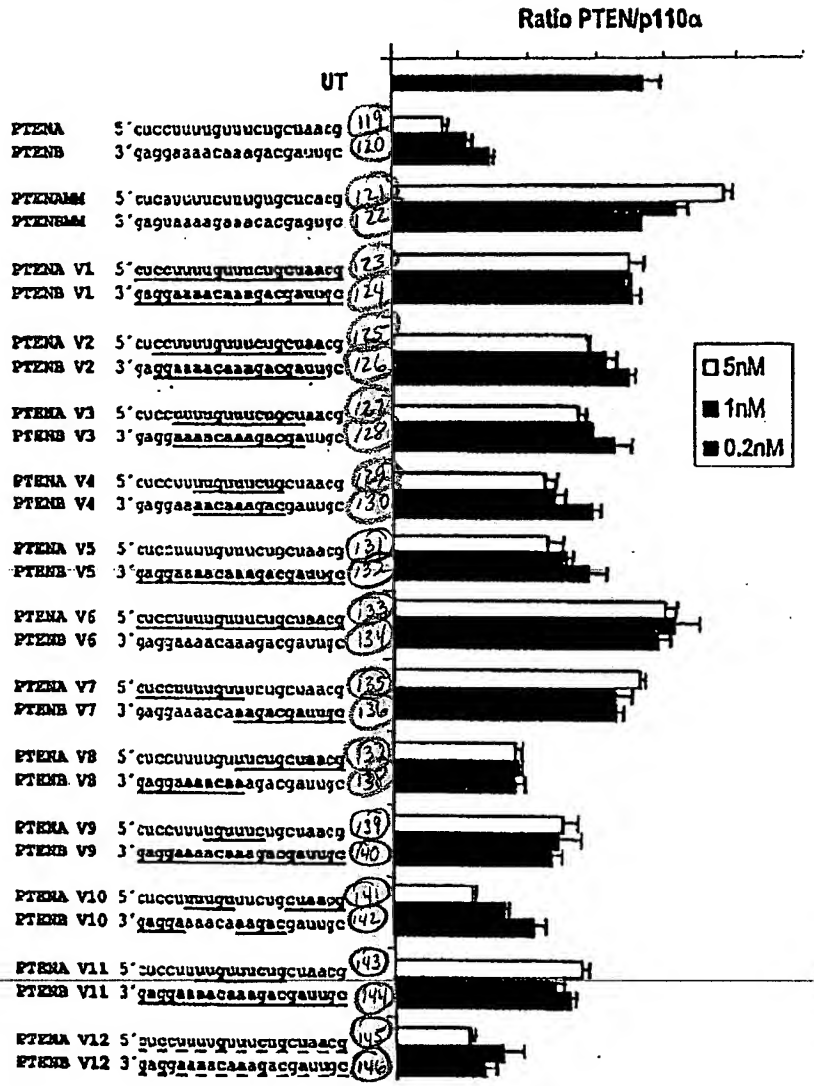

Ratio PTEN/p110α
UT
PTENA 5'cuccuuuuguuucugcuaacg 119
PTENB 3'gaggaaaacaaagacgauugc 120
PTENAMM 5'cucauuuucuuugugcucacg 121
PTENBMM 5'gaguaaaagaaacacgagugc 122
PTENA V1 5'cuccuuuuguuucugcuaacg 123
PTENB V1 3'gaggaaaacaaagacgauugc 124
PTENA V2 5'cuccuuuuguuucugcuaacg 125
PTENB V2 3'gaggaaaacaaagacgauugc 126
PTENA V3 5'cuccuuuuguuucugcuaacg 127
PTENB V3 3'gaggaaaacaaagacgauugc 128
PTENA V4 5'cuccuuuuguuucugcuaacg 129
PTENB V4 3'gaggaaaacaaagacgauugc 130
PTENA V5 5'cuccuuuuguuucugcuaacg 131
PTENB V5 3'gaggaaaacaaagacgauugc 132
PTENA V6 5'cuccuuuuguuucugcuaacg 133
PTENB V6 3'gaggaaaacaaagacgauugc 134
PTENA V7 5'cuccuuuuguuucugcuaacg 135
PTENB V7 3'gaggaaaacaaagacgauugc 136
PTENA V8 5'cuccuuuuguuucugcuaacg 137
PTENB V8 3'gaggaaaacaaagacgauugc 138
PTENA V9 5'cuccuuuuguuucugcuaacg 139
PTENB V9 3'gaggaaaacaaagacgauugc 140
PTENA V10 5'cuccuuuuguuucugcuaacg 141
PTENB V10 3'gaggaaaacaaagacgauugc 142
PTENA V11 5'cuccuuuuguuucugcuaacg 143
PTENB V11 3'gaggaaaacaaagacgauugc 144
PTENA V12 5'cuccuuuuguuucugcuaacg 145
PTENB V12 3'gaggaaaacaaagacgauugc 146
5nM
1nM
0.2nM

Fig. 15

B

PTENA 5'cuccuuuuguuucugcuaacg (119)
PTENB 3'gaggaaaacaaagacgauugc (120)

PTENA V1 5'cuccuuuuguuucugcuaacg (123)
PTENB V1 3'gaggaaaacaaagacgauugc (124)

PTENA V7 5'cuccuuuuguuucugcuaacg (135)
PTENB V7 3'gaggaaaacaaagacgauugc (136)

PTENA V8 5'cuccuuuuguuucugcuaacg (137)
PTENB V8 3'gaggaaaacaaagacgauugc (138)

PTENA V10 5'cuccuuuuguuucugcuaacg (141)
PTENB V10 3'gaggaaaacaaagacgauugc (142)

PTENA V13 5'cuccuuuuguuucugcuaacg (147)
PTENB V13 3'gaggaaaacaaagacgauugc (148)

PTENA V14 5'cuccuuuuguuucugcuaacg (149)
PTENB V14 3'gaggaaaacaaagacgauugc (150)

PTENA V15 5'cuccuuuuguuucugcuaacg (151)
PTENB V15 3'gaggaaaacaaagacgauugc (152)

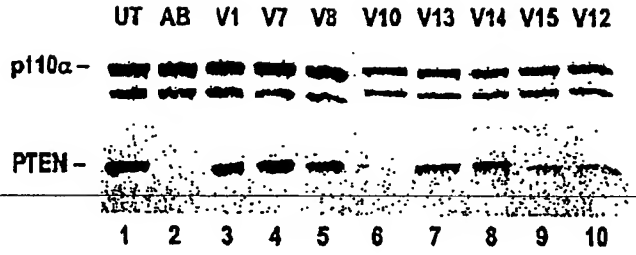
PTENA V12 5'cuccuuuuguuucugcuaacg (145)
PTENB V12 3'gaggaaaacaaagacgauugc (146)

INPUT

15min Serum

2h Serum

C



D

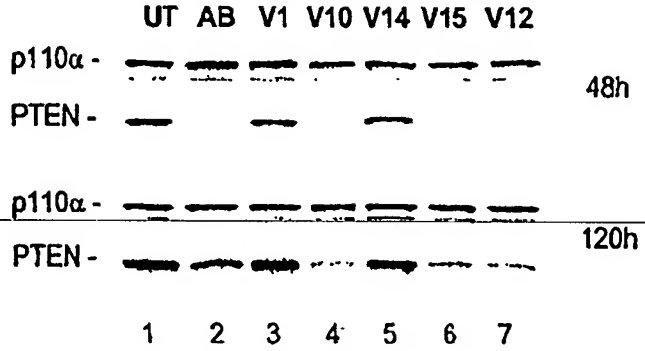
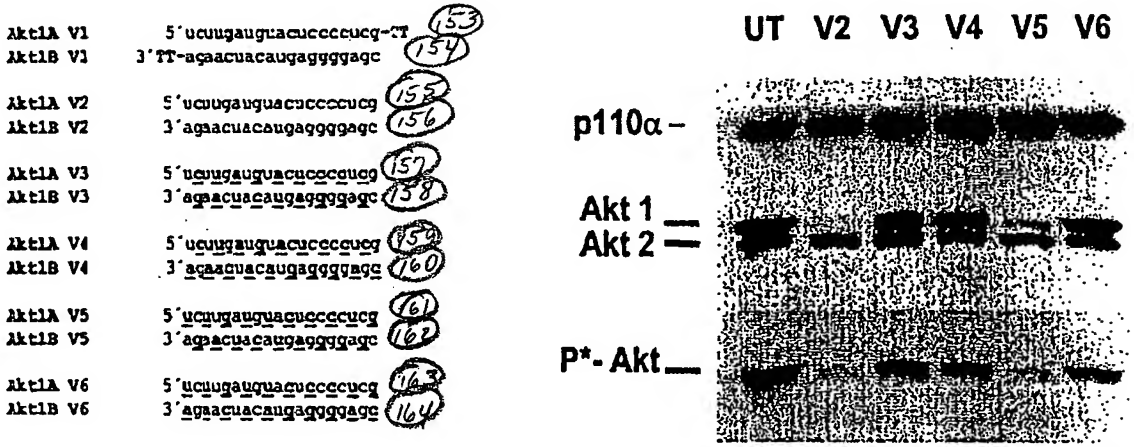


Fig. 15

A


Akt1A V1 5'ucuugauguacucccccucg-TT 153
Akt1B V1 3'TT-agaacuacaugaggggagc 154
Akt1A V2 5'ucuugauguacucccccucg 155
Akt1B V2 3'agaacuacaugaggggagc 156
Akt1A V3 5'ucuugauguacucccccucg 157
Akt1B V3 3'agaacuacaugaggggagc 158
Akt1A V4 5'ucuugauguacucccccucg 159
Akt1B V4 3'agaacuacaugaggggagc 160
Akt1A V5 5'ucuugauguacucccccucg 161
Akt1B V5 3'agaacuacaugaggggagc 162
Akt1A V6 5'ucuugauguacucccccucg 163
Akt1B V6 3'agaacuacaugaggggagc 164
UT V2 V3 V4 V5 V6
p110α –
Akt 1
Akt 2
P*- Akt

B

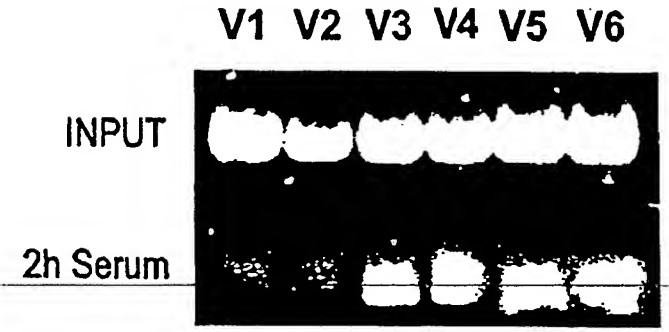

V1 V2 V3 V4 V5 V6
INPUT
2h Serum

Fig. 16

C

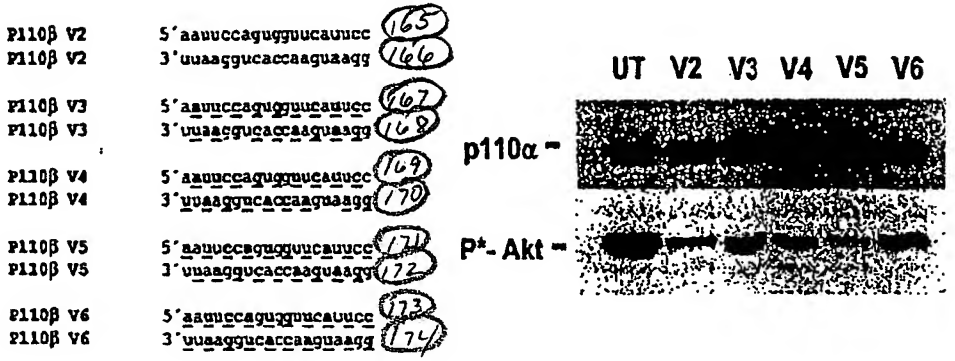
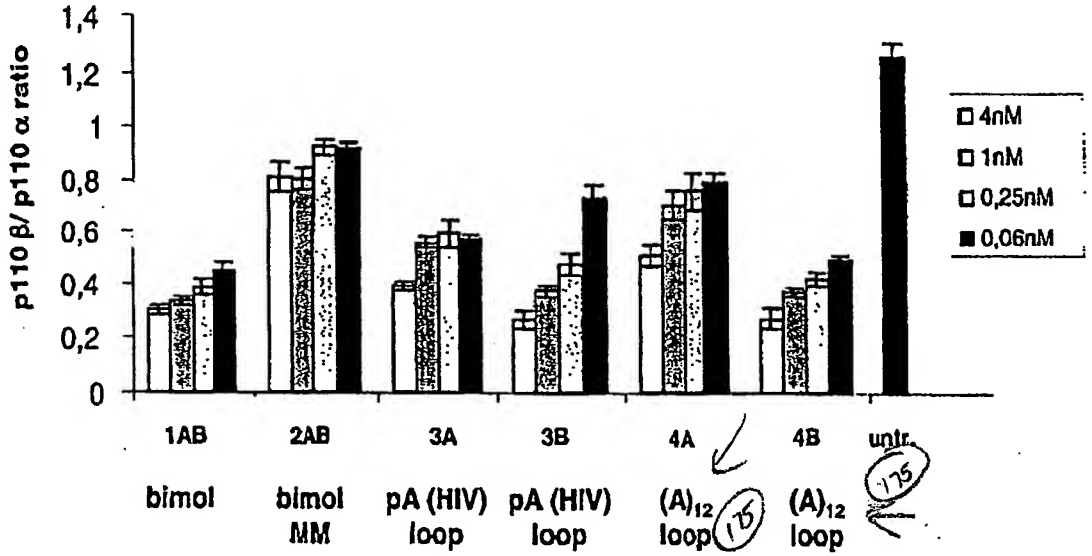

P110β V2
5'aauuccagugguucauucc 165
P110β V2
3'uuaaggucaccaaguaagg 166
P110β V3
5'aauuccagugguucauucc 167
P110β V3
3'uuaaggucaccaaguaagg 168
P110β V4
5'aauuccagugguucauucc 169
P110β V4
3'uuaaggucaccaaguaagg 170
P110β V5
5'aauuccagugguucauucc 171
P110β V5
3'uuaaggucaccaaguaagg 172
P110β V6
5'aauuccagugguucauucc 173
P110β V6
3'uuaaggucaccaaguaagg 174
UT V2 V3 V4 V5 V6
p110α
P*- Akt

Fig. 16

Fig.17

17A



17B

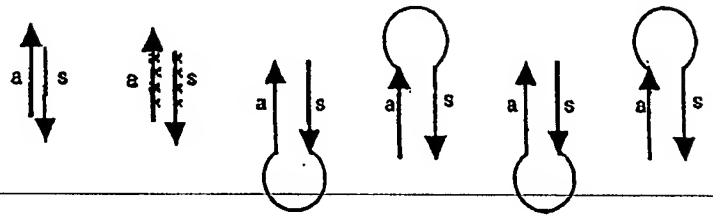
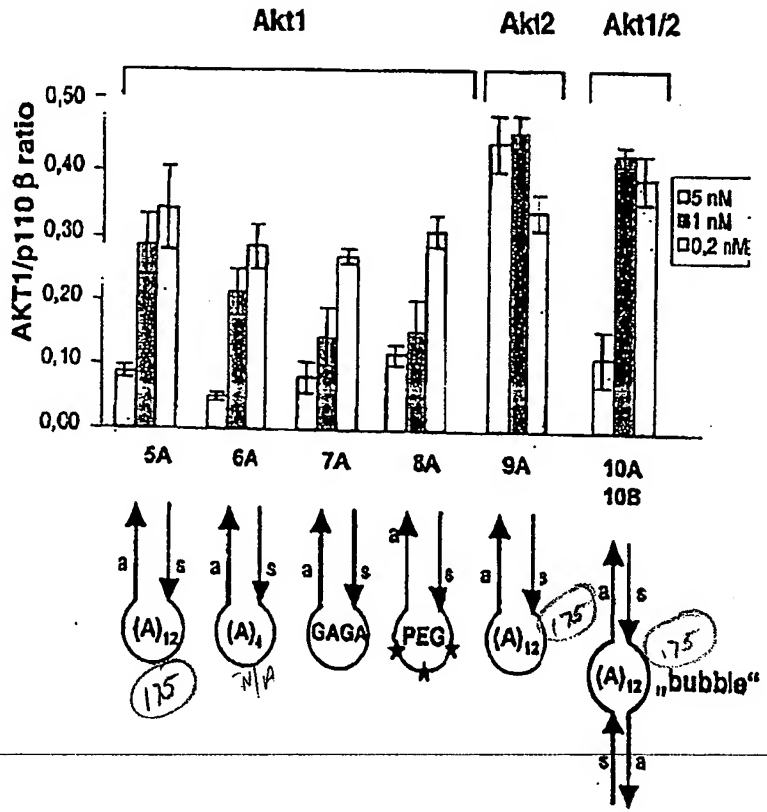


Fig. 18

18A



18B